Cardiorespiratory Effects of Automatic Tube Compensation during Airway Pressure Release Ventilation in Patients with Acute Lung Injury

Hermann Wrigge, M.D.,* Jörg Zinserling, M.Sc.,† Rudolf Hering, M.D.,* Nico Schwalfenberg,‡ Frank Stüber, M.D.,§ Tilman von Spiegel, M.D.,* Stefan Schroeder, M.D.,* Göran Hedenstierna, M.D.,|| Christian Putensen, M.D.#

Background: Spontaneous breaths during airway pressure release ventilation (APRV) have to overcome the resistance of the artificial airway. Automatic tube compensation provides ventilatory assistance by increasing airway pressure during inspiration and lowering airway pressure during expiration, thereby compensating for resistance of the artificial airway. The authors studied if APRV with automatic tube compensation reduces the inspiratory effort without compromising cardiovascular function, end-expiratory lung volume, and gas exchange in patients with acute lung injury.

Methods: Fourteen patients with acute lung injury were breathing spontaneously during APRV with or without automatic tube compensation in random order. Airway pressure, esophageal and abdominal pressure, and gas flow were continuously measured, and tracheal pressure was estimated. Transdiaphragmatic pressure time product was calculated. End-expiratory lung volume was determined by nitrogen washout. The validity of the tracheal pressure calculation was investigated in seven healthy ventilated pigs.

Results: Automatic tube compensation during APRV increased airway pressure amplitude from 7.7 ± 1.9 to 11.3 ± 3.1 cm H₂O (mean ± SD; P < 0.05) while decreasing transdiaphragmatic pressure time product from 45 ± 27 to 27 ± 15 cm H₂O · s⁻¹ · min⁻¹ (P < 0.05), whereas tracheal pressure amplitude remained essentially unchanged (10.3 ± 3.5 vs. 10.1 ± 3.5 cm H₂O). Minute ventilation increased from 10.4 ± 1.6 to 11.4 ± 1.5 l/min (P < 0.001), decreasing arterial carbon dioxide tension from 52 ± 9 to 47 ± 6 mmHg (P < 0.05) without affecting arterial blood oxygenation or cardiovascular function. End-expiratory lung volume increased from 2,806 ± 991 to 3,009 ± 994 ml (P < 0.05). Analysis of tracheal pressure–time curves indicated nonideal regulation of the dynamic pressure support during automatic tube compensation as provided by a standard ventilator.

Conclusion: In the studied patients with acute lung injury, automatic tube compensation markedly unloaded the inspiratory muscles and increased alveolar ventilation without compromising cardiopulmonary function and end-expiratory lung volume.

AIRWAY pressure release ventilation (APRV) ventilates by periodic switching between two levels of continuous positive airway pressure (CPAP) while allowing unsupported spontaneous breathing in any phase of the ventilator cycle. APRV provides adequate ventilatory support in patients with mild pulmonary insufficiency and severe acute lung injury (ALI). In patients with severe ALI, unsupported spontaneous breathing with APRV has been observed to improve ventilation-perfusion matching and arterial blood oxygenation when compared with controlled mechanical ventilation or breath-to-breath inspiratory assistance with pressure support ventilation.

During unsupported spontaneous breathing with APRV, the flow-dependent resistance of the artificial airway (Rₑₑ) imposes an undesirable inspiratory muscle load that may contribute to increased oxygen consumption and patient discomfort. Automatic tube compensation (ATC) provides ventilatory assistance of each spontaneous breath by increasing airway pressure (Pₑₑₑ) during inspiration and lowering Pₑₑₑ during expiration, thereby maintaining calculated tracheal pressure (Pₑₑₑ) constant. Thus, ATC should compensate for Rₑₑ and provide an “electronic” extubation. In patients with increased ventilatory demand or mild pulmonary insufficiency, ATC has been observed to decrease work of breathing and improve patient comfort more effectively than pressure support ventilation or CPAP. However, transient lowering of Pₑₑₑ during ATC to facilitate exhalation should cause a faster decrease of Pₑₑₑ to the preset CPAP level, which may promote alveolar collapse of fast lung compartments and may impair ventilation-perfusion matching in patients with ALI. Although ATC can be used to assist unsupported breaths during partial ventilatory support, its effect on inspiratory muscle load, end-expiratory lung volume (EELV), and gas exchange during APRV has not been assessed in patients with ALI.

The goal of the current study was to investigate, in patients at risk for alveolar collapse, whether spontaneous breathing assisted with ATC during APRV as provided by a standard ventilator will decrease inspiratory muscle load without reducing EELV and impairing gas exchange as a result of a faster decrease in tracheal pressure during expiration. Therefore, we examined cardiopulmonary function in patients with ALI breathing spontaneously during APRV, with and without ATC. To test the efficacy of Pₑₑₑ calculation, measured and calculated Pₑₑₑ were compared in pigs. In patients and pigs, efficacy of dynamic pressure support regulation provided by the used ventilator was examined.
Material and Methods

Patient Investigations

Investigations in patients were performed in the Department of Anesthesiology and Intensive Care Medicine at the University of Bonn, Germany. After approval by the Bonn University Ethics Committee, informed consent for inclusion in the study was obtained from the next of kin of 14 mechanically ventilated patients with ALI.11,12 Patients with a history of chronic lung or heart disease and those with unstable cardiopulmonary function were excluded. Severity of illness was assessed with the Simplified Acute Physiologic Score13 and the Lung Injury Score12 at inclusion in the study.

Routine clinical treatment of the patients included the use of a radial artery catheter and a thermistor-tipped quadruple-lumen pulmonary artery catheter (CCO 746HF8; Baxter Edwards Critical-Care, Irvine, CA).

Cardiovascular Measurements

Heart rate was obtained from the electrocardiogram. Systemic mean arterial pressure, central venous pressure, pulmonary artery pressure, and pulmonary artery wedge pressure were transduced (Combitrans; Braun AG, Melsungen, Germany) and recorded (CS/3, Datex-Engström, Helsinki, Finland). Cardiac output was continuously estimated with the thermal dilution technique (Vigilance, Baxter Edwards Critical-Care). In addition, intermittent determinations of cardiac output were performed using 10 ml of iced 0.9% saline solution as indicator, averaging five determinations performed at random moments during the ventilatory cycle. Standard formulas were used to calculate cardiac index (CI), systemic vascular resistance index, and oxygen delivery index.

Ventilatory and Lung Mechanics Measurements

Gas flow was measured at the proximal end of the endotracheal tube with a heated pneumotachograph (No. 2; Fleisch, Lausanne, Switzerland) connected to a differential pressure transducer (Huba Control, Würenlos, Switzerland). $P_{aw}$ was measured at the proximal end of the endotracheal tube with another differential gas-pressure transducer (SMT, Munich, Germany). Esophageal pressure ($P_{es}$) was measured with a balloon catheter (International Medical, Zutphen, The Netherlands) connected to a differential pressure transducer (SMT). The validity of the esophageal balloon measurements in the supine subject was tested with the occlusion method of Brunner and Wolff.14 Intraabdominal pressure ($P_{ia}$) was measured with a pressure transducer (Combitrans) in the urinary bladder during transient clamping of the Foley catheter after installation of 50 ml saline solution.15 All signals were sampled with an analog–digital converter board (PCM-DAS16S/12, Mansfield, MA) installed in a personal computer. Digitized signals were plotted in real time on the computer screen and stored on magnetic media for offline analysis.

Tidal volume ($V_T$) and minute ventilation ($V_E$) were derived from the integrated gas flow signal and converted to body temperature pressure saturated conditions. Respiratory rate, inspiratory time, and duty cycle (inspiratory time/cycle time) were determined from the gas flow signal. Mean, inspiratory, minimum, and maximum $P_{aw}$ values were determined for each respiratory cycle. Diaphragmatic pressure time product ($PTP_{di}$) was determined from trans-diaphragmatic pressure ($P_{di} = P_{es} - P_{ia}$) as the area under the $P_{di}$–time curve, which was only considered if $P_{di}$ was below a baseline value defined at end expiration to assure that the pressure change resulted from patient activity.16 Spontaneous breaths during APRV may occur on the high or low CPAP levels, as well as during airway pressure release or restoration (fig. 1). Therefore, this $P_{di}$ baseline value was calculated separately for each of the four phases of the mechanical ventilatory cycle (i.e., high CPAP level, low
CPAP level, \( P_{aw} \) release, and restoration of high CPAP level) to compensate for changes in \( P_{di} \) caused by changes in \( P_{aw} \) during APRV. Breaths resulting from restoration of the high CPAP alone, i.e., without detectable deflection in \( P_{es} \) indicating lack of patient activity, were defined as mechanical breaths. Spontaneous breaths were defined as breaths on both CPAP levels during which no step change in \( P_{aw} \) occurred. In an additional analysis, ventilatory variables for these pure mechanical and spontaneous breaths were calculated separately. All ventilatory variables were averaged over a period of 5 min.

Tracheal pressure was continuously estimated as described previously, using the measured gas flow and \( P_{aw} \) tracings as:

\[
P_{tr} = P_{aw} - K_1 \cdot \dot{V}^{K_2}
\]

where \( K_1 \) and \( K_2 \) are tube coefficients describing the nonlinear pressure–flow curve of the tracheal tube. Mean, minimum, and maximum \( P_{tr} \) values were calculated.

Gas Analysis

Arterial blood gases and pH were determined immediately after sampling with standard blood gas electrodes (ABL 620; Radiometer, Copenhagen, Denmark). Oxygen saturation and hemoglobin in each sample were analyzed using spectrophotometry (OSM 3; Radiometer, Copenhagen, Denmark). Fractions of inspired and expired oxygen, carbon dioxide, and nitrogen were measured continuously with mass spectrometry (Random Access Mass Spectrometer M-100; Marquette Hellige, Freiburg, Germany).

Determination of End-expiratory Lung Volume

Multibreath nitrogen washout maneuvers were started consistently from the low CPAP level by changing fraction of inspired oxygen from baseline level to 1.0. Calculation of EELV was described in detail previously. The viscosity-corrected gas flow signal was integrated offline with the measured nitrogen fraction from the beginning to the end of the washout during both inspiration and expiration. The EELV calculation procedure was started with the first oxygen washin breath. As the first breath usually still contains a certain amount of nitrogen, this inspired nitrogen volume was subtracted from the cumulative nitrogen volume calculated from the washout procedure. Mean values of two consecutive EELV determinations were used for the analysis. The coefficient of variation of repeated EELV measurements was 6.8% in this setting.

Protocol

After inclusion into the study, patients remained supine and received continuous infusions of sufentanil and midazolam as necessary, to achieve a Ramsay sedation score of 3. Fluid replacement and infusion of all drugs remained unchanged throughout the study.

Pressure-limited ventilatory support was provided with a demand valve CPAP circuit of a standard ventilator (Evita 4; Dräger, Lübeck, Germany). The low and high CPAP levels were adjusted to a tidal volume of 8 ml/kg and maximum lung compliance, measured during transient apnea induced with repeated intravenous bolus doses of propofol up to a total dose of 2–4 mg/kg. Ventilator rate was set to maintain arterial carbon dioxide tension \( \text{PaCO}_2 \) between 45 and 55 mmHg and fraction of inspired oxygen to maintain arterial oxygen tension greater than 80 mmHg. Ventilator settings were not changed thereafter. During ATC, the ventilator increased \( P_{aw} \) during inspiration and lowered \( P_{aw} \) during expiration to maintain a constant preset \( P_{tr} \). \( P_{tr} \) was estimated by the ventilator as:

\[
P_{tr} = P_{aw} - K_1 \cdot \dot{V}^2
\]

as described previously. An example of \( P_{aw} \), \( P_{es} \), and gas flow tracings during ATC is shown in figure 2. All patients maintained spontaneous breathing during ventilatory support with the settings described above. Patients were assigned to receive APRV with and without ATC in random order. Measurements and data collection were performed during stable conditions confirmed by constancy (± 5%) of \( V_E \), oxygen saturation, expiratory carbon dioxide fraction, mean arterial pressure, and CI for at least 30 min. Before each intervention, the patients’ lungs were inflated manually to an airway pressure of 40 cm \( H_2O \) for approximately 20 s to restore lung history.

Animal Investigations

Investigations in animals were performed in the laboratories of the Department of Clinical Physiology at the University Hospital of Uppsala, Sweden. After obtaining approval from the local animal ethics committee, seven healthy pigs (Hampshire, Yorkshire, and Swedish mixed-country breed; mean weight, 28 ± 4 kg) were studied. Anesthesia was induced with 0.04 mg/kg intramuscular atropine, 6 mg/kg tiletamin–zolazepam, and 2.2 mg/kg xylazin, followed by infusion of 30 mg·kg⁻¹·h⁻¹ ketamine, 0.1 mg·kg⁻¹·h⁻¹ midazolam, and 1–2 µg·kg⁻¹·min⁻¹ remifentanil. The animals were then tracheotomized and ventilated via a cuffed endotracheal tube with an ID of 7 mm (Hi-Contour® 107; Mallinckrodt Medical, Athlone, Ireland). Pigs were breathing spontaneously during APRV with and without ATC on a low CPAP level of 5 cm \( H_2O \) and a high CPAP level of 10 cm \( H_2O \). Ventilatory rate was set at 20 breaths/min with a release time of 1.5 s. \( P_{tr} \) was measured 2–3 cm below the distal end of the endotracheal tube with a fenestrated polyethylene catheter (Erich Jaeger GmbH, Höchberg, Germany) without balloon connected to a differential pressure.
transducer (SMT, Munich, Germany). All other ventilatory and lung mechanics variables were measured or calculated as described above. Measured and estimated $P_{tr}$-time curves were compared by calculating the root mean square of differences.

**Statistical Analysis**

To detect differences in $P_{TP}$, $EELV$, and $CI$ between the ventilatory settings with the given two-sided crossover design at a significance level of 5% ($\alpha = 0.05$) with a probability of 81% ($\beta = 0.19$) based on an estimated difference of 0.82 of the parameter's mean within patient SD, the number of patients to be studied is at least 14.

Results are expressed as mean ± SD. Data were evaluated for normal distribution with the Shapiro-Wilk $W$ test. For comparison of APRV with and without ATC, the $t$ test for dependent samples was used. Differences were considered to be statistically significant at $P < 0.05$.

**Results**

**Animal Study**

The root mean square of differences between measured and calculated $P_{tr}$ was $0.34 ± 0.06$ cm H$_2$O during APRV and $0.41 ± 0.09$ cm H$_2$O during APRV with ATC, indicating a small error for $P_{tr}$ calculation. During ATC, spontaneous inspiratory efforts consistently caused an initial decrease in the measured $P_{tr}$ below the preset CPAP level that was followed by a marked increase of $P_{tr}$ above the preset CPAP level (data not shown). Thus, during ATC, the dynamic pressure support was provided with an average time delay of 166 ± 19 ms by the ventilator.

**Patient Investigations**

The patient's demographic and clinical data are shown in Table 1. Changes in variables reflecting ventilation and respiratory mechanics are given in Table 2. ATC during APRV increased $P_{aw}$ amplitude ($\Delta P_{aw}$, $P < 0.05$) by both lowering minimum $P_{aw}$ ($P < 0.001$) and increasing maximum $P_{aw}$ ($P < 0.001$). The higher $\Delta P_{aw}$ increased $V_{E}$ by approximately 10% ($P < 0.001$), decreased $P_{aCO_2}$ ($P < 0.05$), and reduced inspiratory muscle load as reflected by a decrease in $P_{TPd}$ ($P < 0.05$; Table 3). Although minimum $P_{aw}$ was lowest during APRV with ATC, end-expiratory $P_{aw}$ was not different between the tested ventilatory modalities. ATC increased mean $P_{aw}$ only by a small amount ($19.8 ± 2.9$ vs. $20.1 ± 2.7$ cm H$_2$O; $P < 0.05$), whereas the increase in inspiratory $P_{aw}$ was higher ($21.0 ± 2.7$ vs. $22.4 ± 3.1$ cm H$_2$O; $P < 0.001$). Inspiratory peak flow ($V_{max,i}$) was always higher than expiratory peak flow ($V_{max,e}$). Whereas $V_{max,i}$ increased with ATC ($P < 0.001$), $V_{max,e}$ did not further increase (Table 2). Registrations of estimated $P_{tr}$ indicated an average delay of 159 ± 21 ms of the dynamic pressure support provided by ATC.

Analysis of pure mechanical breaths revealed an increase in $V_{T}$ from $348 ± 157$ to $487 ± 157$ ml ($P < 0.05$), resulting in an increase in $V_{E}$ from $1.7 ± 1.4$ to $3.1 ± 2.3$ l ($P < 0.05$) during ATC. $V_{T}$ of pure spontaneous breaths did not change significantly ($333 ± 273$ ml vs. $361 ± 241$ ml) with ATC.

End-expiratory lung volume increased during ATC from $2.806 ± 0.991$ to $3.009 ± 0.994$ ml ($P < 0.05$; Fig. 4), without affecting arterial oxygen tension/fraction of inspired oxygen (Table 3). All other cardiorespiratory variables remained unchanged throughout the study (Table 3).
Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (yr)</th>
<th>SAPS</th>
<th>LIS</th>
<th>Ventilator Days</th>
<th>Tube (mm)</th>
<th>FIO2</th>
<th>T_high (s)</th>
<th>T_low (s)</th>
<th>CPAP_high (cm H2O)</th>
<th>CPAP_low (cm H2O)</th>
<th>Precipitating Cause of ALI</th>
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<tbody>
<tr>
<td>M</td>
<td>52</td>
<td>11</td>
<td>2.3</td>
<td>12</td>
<td>ET 8.0</td>
<td>0.40</td>
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<td>1.2</td>
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<td>16</td>
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<tr>
<td>F</td>
<td>58</td>
<td>7</td>
<td>2.3</td>
<td>14</td>
<td>ET 7.0</td>
<td>0.30</td>
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<td>7</td>
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<td>13</td>
<td>2.3</td>
<td>4</td>
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<td>15</td>
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<tr>
<td>M</td>
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<td>11</td>
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<td>3.0</td>
<td>3.0</td>
<td>22</td>
<td>15</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>M</td>
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<td>7</td>
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<td>9</td>
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<td>1.0</td>
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<td>18</td>
<td>11</td>
<td>Pneumonia</td>
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<tr>
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<td>2.3</td>
<td>7</td>
<td>ET 7.5</td>
<td>0.35</td>
<td>2.0</td>
<td>0.8</td>
<td>28</td>
<td>18</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>M</td>
<td>65</td>
<td>15</td>
<td>1.7</td>
<td>9</td>
<td>ET 7.5</td>
<td>0.35</td>
<td>3.0</td>
<td>2.0</td>
<td>21</td>
<td>13</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>M</td>
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<td>17</td>
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<td>3.0</td>
<td>1.5</td>
<td>25</td>
<td>15</td>
<td>Abdominal sepsis</td>
</tr>
</tbody>
</table>

SAPS = Simplified Acute Physiologic Score; LIS = Lung Injury Score; FIO2 = fraction of inspired oxygen; T_high, T_low = preset duration of high and low continuous positive airway pressure (CPAP) levels; ALI = acute lung injury; ET = endotracheal tube; TC = tracheal cannula.

Discussion

This study was designed to evaluate the effect of ATC on the cardiorespiratory function in patients with ALI ventilated using APRV. Compensation of the tracheal tube resistance with ATC increased the Paw amplitude by lowering minimum Paw and increasing maximum Paw, thereby augmenting alveolar ventilation and attenuating the patients’ inspiratory muscle load, as reflected by a decrease in PaCO2 and PTPdi.

Despite the transient decrease of Paw to facilitate exhalation, ATC effected no deterioration in EELV or arterial blood oxygenation.

Partial ventilatory support is used increasingly, not only to separate patients from mechanical ventilation, but to provide stable ventilatory assistance of a desired degree during ventilatory failure.1,20–25 During APRV, spontaneous breathing is possible in any phase of the mechanical ventilator cycle,2,24 but spontaneous breaths are mechanically supported only when they coincide with the restoration of the high CPAP level. Therefore, the patient has to overcome the entire load imposed by the resistance of the artificial airway. ATC provides a dynamic assistance of each breath by increasing Paw during inspiration and lowering Paw during expiration to maintain calculated Pes constant at a preset level.3 Thus, ATC minimizes the flow-dependent pressure decrease across the tracheal tube and compensates for Rex. Because the ventilator we used does not generate subambient pressures, expiratory assistance with ATC was provided by transient lowering of Paw below the set CPAP level. Expiratory assistance may become incomplete during ATC with low CPAP levels. In our patients, both the high and the low CPAP levels were markedly positive and thus guaranteed adequate margin for ATC during inspiration and expiration alike.2 Theoretically, during ATC with ideal regulation of dynamic pressure support, the increase in ΔPaw should have resulted in a lower ΔPtr since Pes should not decrease with spontaneous inspiration and should not increase which spontaneous expiration. The observed lack of a decrease in ΔPtr with ATC in our study may be explained by a nonideal regulation of dynamic pressure support by the ventilator.

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Fig. 3. Changes in transdiaphragmatic pressure–time product (PTdi) as an index of patients’ inspiratory muscle load and the airway pressure amplitude (ΔPaw) applied by the ventilator during airway pressure release ventilation (APRV) and APRV with automatic tube compensation (ATC).

Gottfried et al.25 described an algorithm that allows real-time determination of the pressure decrease across the endotracheal tube from gas flow and airway pressure measured at the proximal end of the tracheal tube. The reliability of this algorithm has been confirmed in a mechanical lung model.5 In the ventilator used in this and previous studies,19 a simplified algorithm to estimate P1 during ATC by setting the tube coefficient K2 = 2 was used. Because the expiratory coefficient found by Gottmann et al5 was consistently less than 2, use of the simplified algorithm should result in incomplete compensation of R1 during expiratory ATC for expiratory flows less than 1 l/s. Furthermore, registrations of Paw and estimated and measured P1 indicate that during ATC, dynamic pressure support is provided with a time delay by the used ventilator, thereby resulting in a lack of decrease in ΔP1 (fig. 2). In addition, the algorithm to calculate P1 during ATC is based on ideal laboratory conditions. In patients, effective pressure decrease across the tracheal tube may be underestimated by the ATC algorithm because of changes in the tube geometry from kinking or mucous secretions. Therefore, in the clinical setting, ATC as provided by the used intensive care ventilator does not completely compensate for the resistance imposed by the artificial airway.

Previous investigations have evaluated ATC as a ventilatory support modality in volunteers or ventilated patients during variable ventilatory demand.6,8,19,26,27 In tracheotomized and intubated patients, work of breathing necessary to overcome tracheal tube resistance decreased with ATC compared with pressure support ventilation and CPAP.6,8,26 Similarly, volunteers ranked ATC more comfortable than pressure support ventilation.19,27 Despite the observed advantages of ATC, the transient decrease in Paw that facilitates exhalation may be detrimental to patients at risk for alveolar collapse. Observations in a four-compartment bench lung model indicate that in fast-emptying compartments with low compliance, alveolar pressure may decrease below P1 during early expiration or with short expiratory times.28

Therefore, the faster decline of P1 with ATC during transient decrease in Paw to facilitate expiration may result in lower mean alveolar pressures in fast-emptying lung compartments and may promote alveolar collapse. These observations are supported by findings in pigs with oleic acid lung injury demonstrating rapid increase in atelectasis within 0.6 s during ventilatory support with positive end-expiratory pressure levels less than 20 cm H2O.10

Lowering Paw to facilitate expiration with ATC during APRV in our patients with ALI did not compromise EELV or arterial oxygenation. Surprisingly, EELV even increased in the presence of ATC. This observation may be explained by an unchanged end-expiratory pressure during APRV with and without ATC. Because R4 depends on gas flow, lowering Paw during expiration with ATC is more pronounced during early expiration when gas flow is high. In contrast, ATC has no or only minimal effect on Paw at end expiration, because flow rate at end expiration is minimal even during APRV with variable expiratory times as a result of interfacing of spontaneous breathing. Because Vmax was always higher than Vmax.e and R4 is flow-dependent, R4 should be higher during inspiration than during expiration. Thus, compensation

Table 3. Cardiorespiratory Variables

<table>
<thead>
<tr>
<th></th>
<th>APRV</th>
<th>APRV + ATC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pao2/Fio2 (mmHg)</td>
<td>273 ± 68</td>
<td>293 ± 74</td>
</tr>
<tr>
<td>DO2J (ml · min⁻¹ · m⁻²)</td>
<td>551 ± 47</td>
<td>562 ± 30</td>
</tr>
<tr>
<td>CI (l · min⁻¹ · m⁻²)</td>
<td>3.5 ± 0.5</td>
<td>3.6 ± 0.4</td>
</tr>
<tr>
<td>SVRI (dyne · s · cm⁻⁵ · m²)</td>
<td>1,588 ± 534</td>
<td>1,553 ± 498</td>
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<tr>
<td>HR (min⁻¹)</td>
<td>82 ± 11</td>
<td>86 ± 20</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>82 ± 12</td>
<td>82 ± 12</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>15 ± 6</td>
<td>15 ± 7</td>
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<td>PAP (mmHg)</td>
<td>30 ± 7</td>
<td>28 ± 6</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>14 ± 4</td>
<td>15 ± 4</td>
</tr>
</tbody>
</table>

All values are mean ± SD.

APRV = airway pressure release ventilation; ATC = automatic tube compensation; Pao2 = arterial oxygen tension; Fio2 = fraction of inspired oxygen; DO2J = oxygen delivery index; CI = cardiac index; SVRI = systemic vascular resistance index; HR = heart rate; MAP = mean arterial pressure; CVP = central venous pressure; PAP = mean pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure.
of $R_e$ with ATC resulted in higher mean $P_{aw}$ and may itself cause an increase in EELV. This may be attenuated by differences in inspiratory and expiratory performance of ATC.

Furthermore, ATC resulted in higher inspiratory $P_{aw}$ and maximum $P_{aw}$ during APRV. Pelosi et al. demonstrated in patients with ALI that transient increasing inspiratory plateau pressure from 30 to 45 cm H$_2$O improves EELV and arterial oxygenation. Thus, the observed increase in EELV during APRV with ATC might be partially caused by higher inspiratory $P_{aw}$ and maximum $P_{aw}$.

However, the observed increase in EELV with ATC was not associated with an improvement in arterial oxygenation. Whether this reflects further expansion of already open lung units and no recruitment of collapsed lung tissue remains to be analyzed.

In our patients, ATC during APRV resulted in an increase in $\Delta P_{aw}$ caused by both lowering minimum $P_{aw}$ and increasing maximum $P_{aw}$. Because with ATC the ventilator regulates calculated $P_{r}$ instead of $P_{aw}$, transient increase and decrease of $P_{aw}$ occurs not only during spontaneous breaths but also during the periodic changes of the CPAP levels that constitute APRV. Consequently, ATC during APRV resulted in a higher $\Delta P_{aw}$ and $V_T$ of the mechanical breaths, causing an increase in $V_E$.

The higher $V_E$ and the lower PaCO$_2$ suggest an increase in alveolar ventilation with ATC on condition that ventilatory dead space ventilation and carbon dioxide production remained unchanged. Although previous studies suggested that inspiratory pressure support can decrease carbon dioxide production, this cannot sufficiently explain the decrease in PaCO$_2$ observed in our patients.

In agreement with studies using ATC as primary ventilatory support modality, $V_T$ of the spontaneous breaths did not increase in our patients with ATC. Obviously, our patients reduced their inspiratory effort rather than increased $V_E$ of spontaneous breaths assisted with ATC. This supports the concept that patients have certain ventilatory targets that they try to maintain even if the ventilatory assistance changes within a certain range.

During APRV, ATC consistently decreased $P_{TP,di}$ as an index for inspiratory muscle load by 40%. Similar reduction in work of breathing has been found previously during spontaneous breaths assisted with ATC. This reduction of inspiratory effort with ATC seems to be relatively high. However, even in patients with obstructive lung disease and high airway resistance, $R_e$ can be the major component of total resistance. If $V_E$ and, consequently, inspiratory flow is high, the share of total resistance that $R_e$ constitutes further increases because of the nonlinear dependency of $R_e$ on gas flow. This may explain the marked reduction of the inspiratory effort in the presence of ATC in our patients who had a high $V_E$ and respiratory rate. In agreement with our findings, ATC has been observed to provide better unloading from the undesirable load because of $R_e$ than constant pressure support or CPAP in patients with increased ventilatory demand. Furthermore, investigations in healthy volunteers suggest that the comfort of breathing depends on both the inspiratory and expiratory assistance during ATC.

In our patients, spontaneous breathing assisted with ATC during APRV was not associated with a decrease of CI, although $\Delta P_{aw}$ was significantly lower. Periodic decrease in intrathoracic pressure during spontaneous inspiration with APRV has been suggested to improve venous return and CI. Apparently, during APRV with ATC, spontaneous respiratory activity decreased intrathoracic pressures sufficiently to cancel out the cardiovascular depression caused by higher airway pressures and reduction in $\Delta P_{aw}$.

The results of this study demonstrate that despite the observed nonideal regulation of dynamic pressure support, ATC during APRV in our patients with ALI unloaded considerably the inspiratory muscle load and increased alveolar ventilation without compromising cardiorespiratory function. Transient lowering of $P_{aw}$ during expiration with ATC did not promote alveolar collapse in these patients. Further studies are warranted to evaluate these and previous observations with respect to clinical relevance.

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